Appendiceal Nodules in the Setting of Endometriosis Can Be Carcinoid Tumors

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ABSTRACT

Introduction: Endometriosis is occasionally found in the appendix, particularly in severe forms of deep infiltrating disease. Carcinoid tumor is the most common neoplasm of the appendix and may be overlooked or misdiagnosed when there are multiple endometriosis lesions in the pelvis.

Case Description: We describe two cases of carcinoid tumor diagnosed in patients who underwent surgery to treat endometriosis, in whom the diagnosis of appendiceal endometriosis was presumed.

Discussion: In the context of endometriosis, surgery is indicated when the appendix is affected. Despite the more likely diagnosis of appendiceal endometriosis, carcinoid tumors cannot be ruled out by imaging examinations.

Key Words: Appendiceal neoplasm, Appendix, Carcinoid tumor, Endometriosis.

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INTRODUCTION

Endometriosis is a common benign disease found in up to 15% of women of reproductive age and associated with chronic pelvic pain and infertility.[1,2] Deep infiltrative endometriosis (DIE), the most severe type, often affects the bowel, particularly the rectosigmoid colon,[3] and occasionally may be found in the appendix.[4] The bowel is involved in 5.4–25.4% of cases of endometriosis.[5] The rectosigmoid colon is the most frequently affected segment of the bowel, followed by the ileum and appendix.[6,7] Depending on the population studied, endometriosis is found in the appendix in 0.4– 22% of cases. The percentage is higher in patients with more severe disease or lesions at multiple sites.[8]

Carcinoid tumor is the most common neoplasm of the appendix, with an incidence of 0.32% in appendectomy specimens of both sexes[9] and 0.054% in autopsy series.[10] Appendiceal carcinoid tumors comprise 18.9% of all gastrointestinal carcinoid tumors, but they are less biologically aggressive. The typical appendiceal carcinoid is situated at the tip of the appendix and is smaller than 2 cm at presentation. Most patients are asymptomatic. These lesions are usually found at surgery performed for symptoms of acute appendicitis or during incidental appendectomy.[11,12] Patients with appendiceal carcinoids are younger at presentation (mean age, 42.2 years) than patients with other gastrointestinal carcinoid tumors (62.9 years) or noncarcinoid appendiceal tumors (61.9 years), and they have a tendency to present with multiple primary tumors. Metastatic potential is low. These neoplasms have a female predominance, with a female/male ratio of 2.13.[13,14]

This report describes 2 cases of carcinoid tumor diagnosed in patients who underwent surgery for treatment of DIE, in whom the presumptive preoperative diagnosis was appendiceal endometriosis.

CASES

Between July and December 2013, 108 patients with a diagnosis of DIE underwent surgical treatment in our center. All patients had undergone prior mapping of the endometriosis lesions (after bowel preparation), by transvaginal and transabdominal pelvic ultrasonography with a high-resolution linear transducer, by magnetic resonance imaging (MRI) of the pelvis, or by both.[15–17] Surgery is indicated in cases refractory to at least 6 months of medical management and in cases with specific lesions such as ovarian endometriomas exceeding 4 cm; lesions in the ileum, cecum, appendix, or urinary tract; and large lesions of the rectosigmoid colon, posing a risk of obstruction.

Findings and Description of Cases

Imaging studies in 108 patients identified lesions in the appendix in 6 (5.5%). The appendix was resected as part of the surgical management of the endometriosis. Histologic evaluation of the 6 appendix specimens revealed that 4 contained endometriotic lesions, whereas 2 contained carcinoid tumor.

Case 1. A 36-year-old woman was referred to our center after diagnosis of DIE as an incidental finding in an MRI of the abdomen performed as part of the investigation of a pulmonary embolism. She reported having had severe dysmenorrhea, dyspareunia, and cyclic dyschezia for years, but no investigation for endometriosis had been conducted. She had been sexually inactive for 2 years due to severe pain during intercourse and had initiated use of a contraceptive ring to alleviate symptoms of premenstrual disorder 2 months before the diagnosis of the pulmonary embolism.

After the MRI revealed DIE, a work-up for endometriosis included transvaginal and transabdominal pelvic ultrasonography (after bowel preparation) which showed a 2-cm lesion suggestive of DIE affecting the rectosigmoid colon, a 3-cm lesion in the retrocervical region, and a 2.4-cm nodule in the tip of the appendix. These findings were also seen on the MRI. The appearance of an appendiceal nodule was not typical of endometriosis in either imaging study, because it had well-defined edges and was hypervascularized. Surgery was indicated based on the failure of medical treatment to control the symptoms and because of the presence of the appendiceal nodule (**Figure 1**). During the laparoscopy, multiple adhesions involving the ovaries, fallopian tubes, rectosigmoid colon, and retrocervical region, as well as the lesions identified by transvaginal ultrasonography and MRI were visualized. Surgical treatment consisted of adhesiolysis, resection of the retrocervical nodule, appendectomy, and discoid resection of the rectosigmoid lesion with a circular stapler.

Histological analysis confirmed the diagnosis of DIE in all resected sites except the appendix. The appendiceal nodule was diagnosed as a well-differentiated carcinoid tumor involving all layers of the appendix, with extension to the adjacent connective and adipose tissue and perineural infiltration.

Case 2. A 32-year-old woman with a history of previous treatments for endometriosis including 2 laparoscopies and use of a gonadotropin-releasing hormone (GnRH)

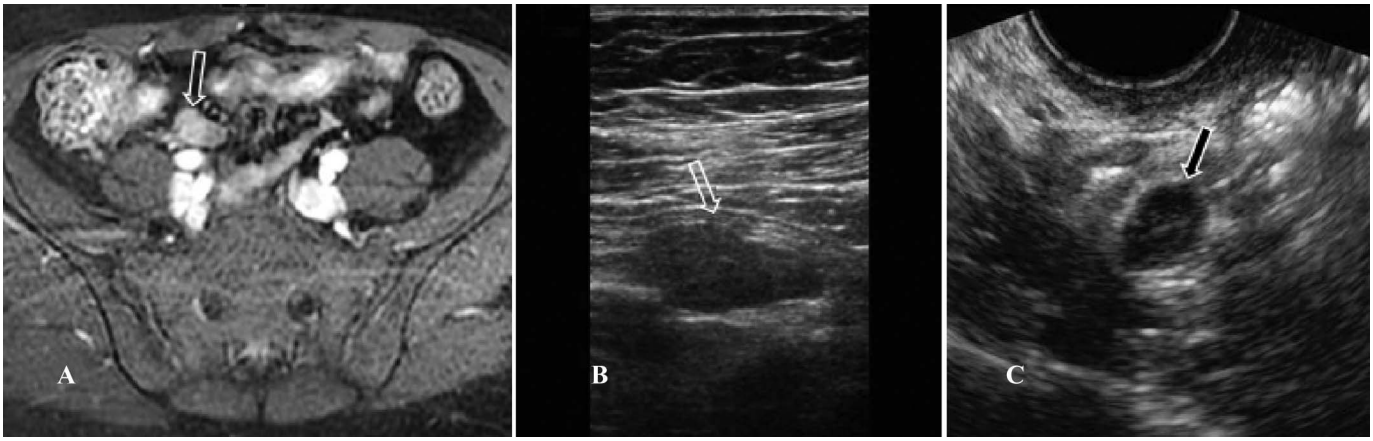

Figure 1. Hypervascular solid nodule at the tip of the appendix (arrows). *A*, Postcontrast axial T1 MRI with fat suppression. *B*, Transabdominal ultrasonography with high-resolution linear transducer. *C*, Transvaginal ultrasonography.

analogue had an infertility diagnosis and had attempted in vitro fertilization twice. One year earlier, she had had an ectopic pregnancy requiring right salpingectomy. Although she had undergone prior treatments, she continued to experience severe symptoms of dyspareunia, acyclic pelvic pain, dysmenorrhea, and dyschezia. After she was referred to our center, transvaginal and transabdominal ultrasonography after bowel preparation showed multiple lesions of endometriosis, including a 7-cm endometrioma in the right ovary, 3 nodules involving the rectosigmoid colon, and a 4-cm lesion involving the vagina and retrocervical region. The appendix was unremarkable. The indication for surgery was based on symptoms, the size of the ovarian endometrioma, and the failure of 2 cycles of in vitro fertilization (**Figure 2**).

During laparoscopy, extensive adhesions involving the ovarian endometrioma, rectosigmoid colon, and appendix were observed, all adherent to the retrocervical region. Because the appendix had an atypical appearance and was attached to the other endometriotic lesions, an appendectomy was performed. Surgical treatment consisted of adhesiolysis, appendectomy, segmental resection of the rectosigmoid colon, and resection of the endometrioma capsule and lesions in the retrocervical region, vagina, and uterosacral ligaments.

The histological evaluation unexpectedly showed a 7-mm neuroendocrine neoplasm in the appendix, with vascular invasion and involvement of the mesoappendix. All the other sites resected were confirmed to be endometriosis lesions (**Figure 3**).

Follow-up and Outcomes

Given the extension of the appendiceal neoplasms to the adjacent connective and adipose tissue and perineural infiltration in the first case and the vascular invasion and involvement of the mesoappendix in the second one, both patients subsequently underwent uneventful laparoscopic right colectomies. Histological evaluation of the 2 colectomy specimens established that there was no residual tumor or regional lymph node involvement. The patient in the first case underwent surgery in August 2013. One and a half years later, she was well, asymptomatic, and using a levonorgestrel intrauterine system for contraception. The patient in the second case underwent surgery in November 2013, became pregnant in January 2014, and had a Cesarean delivery in October 2014. As of February 2015 she was continuing to breast-feed her infant and was taking oral desogestrel for contraception.

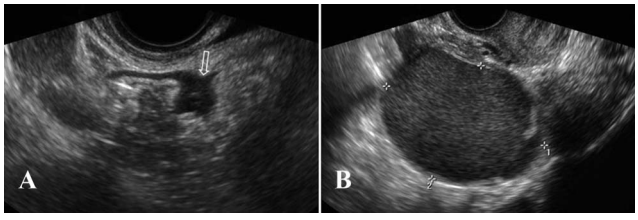

Figure 2. Transvaginal ultrasonography. *A*, DIE of the sigmoid colon, with focal thickening of the muscularis propria (arrow). *B*, Endometrioma of the right ovary.

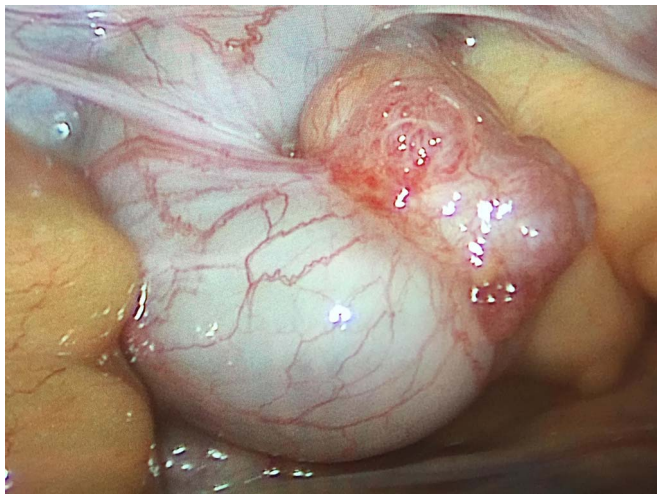

Figure 3. J-shaped appendix with a nodular lesion at the tip.

DISCUSSION

As a referral center for the treatment of endometriosis, our service performs several surgical procedures for the treatment of endometriosis and sees a large number of patients with advanced-stage disease. This referral bias most likely explains the relatively high incidence of lesions of the appendix found in our series (6/108; 5.5%). Four of the 6 cases (3.7%), the appendiceal lesions were indeed endometriosis, and 2 (1.8%) they were carcinoid tumors.

Several reports have noted the importance of specialized imaging, particularly transvaginal ultrasonography and MRI, for the mapping of endometriosis lesions.[15–17] Our imaging protocol includes evaluation of the right iliac fossa with a high-resolution linear transducer, to detect lesions of the ileum, cecum, and appendix. In most cases, detection of endometriosis lesions in these topographies is feasible, but in the case of the appendix, the diagnosis of carcinoid tumors cannot be ruled out.

Thus, during laparoscopic surgery for endometriosis, the appendix should always be inspected and resected if any abnormalities, such as the presence of nodules, thickening, swelling, or adhesions suggestive of disease, are

found. Patients with cyclic bowel symptoms, advanced stages of disease, and endometriotic lesions at multiple sites are at higher risk of having the appendix affected by endometriosis.[4] A carcinoid tumor may be unexpectedly diagnosed in an appendiceal lesion thought to be endometriosis. Elective coincidental appendectomy in patients who have chronic pelvic pain or endometriosis was endorsed in a 2005 American Congress of Obstetricians and Gynecologists (ACOG) Committee on Gynecologic Practice Opinion and was reaffirmed in 2014.[18]

The prognosis for patients with a conventional appendiceal neuroendocrine neoplasm is good, and the 5-year survival rate exceeds 95%. Lymph node metastasis to regional lymph nodes and distant metastasis occur in approximately 4% and 1% of cases, respectively, usually when the primary tumor is larger than 2 cm. Treatment by appendectomy is curative in most cases, particularly for tumors smaller than 1 cm. In cases with lymph node metastasis, tumor size exceeding 2 cm, presence of regional lymph node metastasis, high mitotic count, mesoappendiceal invasion, or peritoneal studding or angioinvasion, a right hemicolectomy is advised. If the proximal resection margin alone is involved, conservative local re-excision may be considered.[19]

Appendiceal lesions may be found in up to 22% of women with DIE, particularly when multiple sites are affected.[14] Despite the more likely diagnosis of endometriosis of the appendix, carcinoid tumors cannot be ruled out by imaging examinations. Our cases emphasize the need to approach these lesions carefully and strengthens the indication for appendectomy when the appendix is affected in the setting of endometriosis.

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